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ETHICALITY AND APPLICATIONS OF CRISPR-CAS9 TECHNOLOGY

Anjali Phadnis

Research Scholars Program, Harvard Student Agencies, In collaboration with Learn with Leaders.

ABSTRACT

Novel CRISPR-Cas9 technology has come to the forefront of the biomedical field, with the potential to make revolutionary changes to healthcare. Diseases that currently have no cure may see a brighter outlook in the future due to this development. However, ethical challenges including germline editing and bioterrorism must be taken into consideration before the technology becomes widespread. Using the examples of treatment for Multiple Sclerosis, lung cancer, and Alzheimer's, it is clear that the usage of CRISPR-Cas9 will revolutionize medicine and have significant benefits as long as the technology remains under regulation.

KEYWORDS: CRISPR, Cas9, CRISPR-Cas9, Genetics, Genome, Biotechnology

INTRODUCTION

Genome editing allows researchers to edit DNA through the insertion, excision, or alteration of genetic material across the genome. Genome editing has become a prevalent topic in biomedical research as it has the capability to prevent and treat diseases. CRISPR-Cas9 (Clustered Regularly Interspaced Short Palindromic Repeats and CRISPR-associated protein 9) is of most interest in genome editing. CRISPR-Cas9 is "faster, cheaper, more accurate, and more efficient than other genome editing methods" ("What are genome editing and CRISPR-Cas9?", n.d.). However, researchers are reviewing the safety and ethicality of this revolutionary technology.

Currently, the technology is only in use at research labs where it is being tested on cells and animal models. A major cause of this is the ethical issues that arise when applying CRISPR-Cas9 to human genomes. Most genomic editing is limited to somatic cells, which are not germline cells. However, changes made to germline cells have the potential to impact the genetic makeup of future generations ("What are genome editing and CRISPR-Cas9?", n.d.). This brings up medical and ethical dilemmas due to the possibility of misuse. Other concerns arise in relation to bioterrorism as CRISPR-Cas9 has the ability to alter pathogens and potentially make them more harmful to entire populations. Yet, gene editing also has the potential to improve the medical field and enhance treatments for a variety of diseases, including Multiple Sclerosis (MS), lung cancer, and Alzheimer's. The use of CRISPR-Cas9 will enhance quality of life through novel treatments and more personalized medicine. Further uses must be thoughtfully regulated to prevent ethical issues from arising.

Materials & Methods

Significant research was conducted to weigh the ethicality of CRISPR-Cas9 technology. Secondary research was utilized to evaluate potential uses of genomic editing in various case studies as well as its impacts on society.

Results & Discussion

CRISPR-Cas9 Technology

The origins of CRISPR-Cas9 technology come from prokaryotes, organisms that lack a nucleus. This means these organisms have DNA throughout their cytoplasm. Due to this distinct feature, prokaryotes have an efficient method of "detecting and neutralizing foreign genes that could prove their undoing" (Tregaskis, 2020). Each time the organism undergoes this process, it captures a few clustered regularly interspaced short palindromic repeats and creates an RNA copy. As the immune system protects the cytoplasm, it detects these. If it recognizes a foreign gene, it uses a CRISPR-associated protein (Cas) to break the DNA and protect itself (Tregaskis, 2020).

In the case of eukaryotes, including humans, this process is much more difficult. Eukaryotic cells contain nuclei to hold DNA. Using a combination of advanced technology, researchers have figured out how to get past the cellular membrane and into the nucleus to alter DNA. Recent technological innovations have improved control over this process, allowing researchers to turn target genes on and off. CRISPR has been revolutionary in permitting researchers to alter DNA at specific locations. They use CRISPR RNA with pieces of the target gene sequence, then inject it with a Cas enzyme into the nucleus. The Cas enzyme finds the desired location and induces double-strand breaks. This technology has transformed the biomedical field and scientists' understanding of various diseases. It has opened opportunities for significant advancements (Tregaskis, 2020).

Treatment of Multiple Sclerosis

Multiple Sclerosis (MS) is categorized as an autoimmune disease, a disorder in which the body's own immune system disrupts its tissues. Gene therapy has become a hopeful approach to treating these disorders. Four studies tested genetic therapy in human cell models in MS. From these studies, various genes have been suggested to have a link to the development of MS. These genes are appropriate candidates for CRISPR-Cas9 treatment (Lee et al., 2022). Multiple Sclerosis is a disorder that damages the central nervous system. Many people that suffer from MS are not able to have a quality of life up to its full potential. With these technological advancements, a previously chronic condition may have the possibility of being cured.

Treatment of Lung Cancer

In the case of lung cancer, an incurable disease, CRISPR-Cas9 has two approaches for treatment. "The first approach involves creating single directed RNA and Cas9 proteins and then distributing them to cancer cells using suitable methods. Single directed RNA looks directly at the lung's mutated epidermal growth factor receptor and makes a complementary match, which is then cleaved with Cas9 protein, slowing cancer progression. The second method is to manipulate the expression of ligand-receptors on immune lymphocytic cells. For example, if the CRISPR-Cas9 system disables the expression of cancer receptors on lymphocytes, it decreases the contact between the tumor cell and its ligand-receptor, thus slowing cancer progression" (Tiruneh et al., 2021). This personalized medicine has the potential to improve the outlook of many patients' lives. A cancer diagnosis is devastating and impacts millions yearly. With the possibility of unprecedented cancer treatment, the usage of CRISPR-Cas9 technology is worth any possible risks that can be mitigated, providing cancer patients with hope for a better future.

Treatment of Alzheimer's Disease

Many neurodegenerative disorders, most commonly Alzheimer's, lack treatments to cure or even slow progression of the disorder. Recent clinical trials have not resulted positively, suggesting the need for novel technology. Alzheimer's disease entails the accumulation of tau and amyloid-β (Aβ). Recently, CRISPR-Cas9 technology has been used to create new Alzheimer's models that show a more accurate representation of the disease and find a therapy that treats tau and Aβ (De Plano et al. 2022). This debilitating disease devastates quality of life for its victims. With new technology available to treat Alzheimer's, it is highly plausible that millions of lives could change for the better.

Ethical Concerns

Inevitably, ethical concerns arise when it comes to editing human genomes. Safety is at the forefront as misuse of the technology can create lasting devastation. Ethicality was discussed at the International Summit on Human Gene Editing. It was agreed upon that germline genome editing should not be used for clinical reproductive purposes as "the risk cannot be justified by the potential benefit" ("What are the Ethical Concerns of Genome Editing?", 2017). Germline editing is controversial and debated upon. It has the potential to improve lives for generations, especially if both parents are homozygous for a disease-causing variant (both parents have two copies of the variant, meaning all of their children would carry the disease) ("What are the Ethical Concerns of Genome Editing?", 2017). However, if misused, this can lead humanity down a slippery slope to genetically engineering future generations. Additionally, CRISPR technology can theoretically be used for bioterrorism. The 20th century brought biological weapons, and this technological advancement has the potential to bring more. Many nations are ill-equipped to handle bioterrorist attacks; thus, the potential risk associated with

this is very high (Cropper, 2020). Hypothetically, gene editing can be used to alter pathogens and make them deadlier for mass destruction in wartime.

CONCLUSION

CRISPR is undeniably a revolutionary advancement, with its applications having the ability to treat a myriad of diseases. The positive results that can be achieved outweigh potential worries. The ethical concerns that arise are more theoretical than the positive impacts that can be directly achieved. Therefore, mindful regulation can be placed to mitigate these repercussions before they become reality. These regulations must be effectively and openly discussed before CRISPR technology can be put into use. With a proper system in place to review its uses, gene editing will only be used to foster health, rather than being used for unethical purposes. CRISPR-Cas9 technology will enhance the health and livelihood of many through novel treatments and more personalized medicine.

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